UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,576	06/29/2005	Toshitada Noguchi	2005_0034A	4025

513 7590 03/16/2010

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
03/16/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

Office Action Summary	Application No.	Applicant(s)	
	10/521,576	NOGUCHI ET AL.	
	Examiner	Art Unit	
	Kade Ariani	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,8 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 5, 8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on August 13, 2009 has been received and entered.

Claims 3, 4, 6 and 7 have been canceled.

Claims 2, 5, 8, and 9 are pending in this application and were examined on their merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/13/2009 has been entered.

Declaration under 37 C.F.R. § 1.132

The declaration of Tomoki Hamamoto under 37 CFR 1.132 filed on 03/30/2009, and Applicant's arguments filed on 08/13/2009 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5, 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 5 reads "adding … N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), and … N-acetylneuraminic acid lyase (NeuAc lyase)… to a reaction system containing N-acetylglucosamine (GlcNAc)…." . This is confusing and render the claims indefinite because,

According to IUBMB enzyme nomenclature for EC 4.1.3.3, N-acetylneuraminic acid lyase convert N-acety-D-mannosamine and pyruvate to N-acetylneuraminate or N-acetylglucosamine and if you add pyruvate then you will end up with N-acetylneuraminate or N-acetylglucosamine, and according to the previously cited IUBMB enzyme nomenclature for EC 5.9.3.1, the substrate of the enzyme N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase) is N-acetylglucosamin-6-phophate not N-acetylglucosamine (or GlcNAc). Therefore, assuming that the starting material is N-acetylglucosamine (GlcNAc), is not exactly clear how N-acetylglucosamine (GlcNAc) which is not the substrate of the enzyme N-acetylglucosamine-6-phosphate 2-epimerase, is being converted to the final product

since the sequence of the reactions in the claimed process is/are not clear. Applicant should amend to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koizumi et al. (US 2002/0064836 A1) in view of Plumbridge & Vimr (Journal of Bacteriology, 1999, Vol. 181, No.1. p47-54), and further in view of Tabata et al. (Enzyme & Microbial Technology, March 2002, Vol. 30, p.237-333), and further in view of IUBMB enzyme nomenclature (EC 5.9.3.1), is withdrawn due to Applicant's amendments to the claims.

Claims 2, 5, 8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishige et al. (in IDS, Biosci. Biotechnol. Biochem., 2001, vol. 65, No.8, p.1736-1740) in view of Kohno et al. (Agric. Biol. Chem., 1983, Vol. 47, No.1, p.19-24) and Rodriguez-Aparicio et al. (Biochimica et Biophysica Acta, 1999, Vol. 1428, p.305-313)

and further in view of Tabata et al. (Enzyme & Microbial Technology, March 2002, Vol. 30, p.237-333).

Claims 2 and 8 are drawn to a process which comprises adding 2-100 mg/ml N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), and 2-100 mg/ml N-acetylneuraminic acid lyase (NeuAc lyase), to a reaction system containing N-acetylglucosamine (GlcNAc), pyruvate, and subsequently adding 1-20% yeast cells, and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase), and cytidine 5'-monophosphate (CMP), and thereby synthesize CMP-NeuAc, the process further comprising adding an inorganic phosphoric acid, magnesium and an energy source to the reaction system.

Claims 5 and 9 are drawn to a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc), comprises adding 1-20 % yeast cells, 2-100 mg/ml N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), 2-100 mg/ml N-acetylneuraminic acid synthase (NeuAc synthase), and 2-100 mg/ml CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase) to a reaction system containing N-acetylglucosamine (GlcNAc) and cytidine 5'-monophosphate (CMP), and inducing reaction of the mixture, the process further comprising adding an inorganic phosphoric acid, magnesium and an energy source to the reaction system.

Ishige et al. teach a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc) comprising using CMP-NeuAc synthetase which catalyzes cytidylylation of N-acetylneuraminic (or NeuAc) using CTP as cytidylyl donor (p.1738 1st column 3rd paragraph lines 1-3). Ishige et al. teach using CTP as a cytidylyl donor is expensive,

however yeast cells can be used as CTP-generating system (p.1736 Introduction 2nd column 1st paragraph lines 1-2 and 8-9). Ishige et al. also teach a CTP-generating system and an inorganic phosphate can be used (Abstract).

Ishige et al. do not teach adding 2-100 mg/ml N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), and 2-100 mg/ml N-acetylneuraminic acid lyase (NeuAc lyase), to a reaction system containing N-acetylglucosamine (GlcNAc) and pyruvate, 2-100 mg/ml N-acetylneuraminic acid synthase (NeuAc synthase), and adding 1-20% yeast cells, and further adding magnesium and an energy source. However, Kohno et al. teach yeast enzyme pyrimidine nucleoside monophosphate kinase is able to generate CTP using CMP, and the specific activity of the enzyme (in units/mg), the enzyme using ATP energy source and requires divalent cations Mg^{+2} (see Abstract, p. 20 Table I. 3rd column 1st row, and p. 21 2nd column last paragraph line 1, and p.22 2nd column 2nd paragraph lines 1-4). Therefore, since the at the time the invention was made the specific activity of the enzyme of the yeast cells were known in the art the amount of yeast cells to be added to the reaction would be considered obvious absence of evidence to the contrary.

Moreover, Rodriguez-Aparicio et al. teach producing N-acetylneuraminic acid or NeuAc using N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase) and N-acetylneuraminic acid lyase (NeuAc lyase) to a reaction system containing N-acetylglucosamin-6-phophate (GlcNAc-6-phophate) and pyruvate to synthesize N-acetylneuraminic acid (Neu5Ac) (p.307 2nd column 4th paragraph lines and p.311 2nd column 2nd paragraph Steps I and II). Rodriguez-Aparicio et al. further teach the specific

activity of the each unit of enzyme is defined as the amount of N-acetylglucosamine-6-phosphate 2-epimerase that synthesizes 1 nmol of ManNAc-6-phsophate per minute at 37°C under assay conditions (p.308 1st column 2nd paragraph). Rodriguez-Aparicio et al. also teach NeuAc lyase stoichiometrically transforms the ManNAc generated to NeuAc, and 0.05U of NeuAc lyase completely transformed the ManNAc to Neu5AC (or NeuAc) (p.308 2nd column 5th paragraph lines 1-2, and p.309 1st column 2nd paragraph lines 9-12). Therefore, since at the time the invention was made the specific activity of the enzymes were known in the art the amount of enzymes to be added to the reaction would be considered obvious absence of evidence to the contrary.

Tabata et al. teach producing NeuAc using N-acetylneuraminic acid synthase (or NeuAc synthase) the enzyme is able to produce NeuAc from ManNAc (p.327 Introduction 2nd column 1st paragraph lines 2-3 and p.331 2nd column 4th paragraph lines 11-15).

Therefore, a person of ordinary skill in the art at the time the invention was made, would have been motivated to apply the prior art teachings in the method as taught by Ishige et al. in order to provided a process for producing CMP-N-acetylneuraminic acid with a reasonable expectation of success, because Rodriguez-Aparicio et al. teach producing N-acetylneuraminic acid using N-acetylglucosamine-6-phosphate 2-epimerase and N-acetylneuraminic acid lyase and because Tabata et al. teach producing NeuAc using N-acetylneuraminic acid synthase is able to produce NeuAc from ManNAc.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on IFP.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651